

Appl. No.: 10/076,727
Amdt. Dated: 10/3/2005
Off. Act. Dated: 8/3/2005

Amendments to the Claims

Claims 7-10, 14, 17, 19, and 20 have been amended to better point out the doped lipid bilayer nature of membranes in this Application. Support for these amendments are found *inter alia* at the last sentence of the Abstract, paragraph [0088], which states:

"The lipid bilayer membranes are doped with various lipids and/or proteins to modulate the adherence of the cells being used in the device."

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Cancelled) A micro-array device for determining adherence of selected cells contacting the device to a lipid membrane of the device, comprising:
 - a. an inert solid substrate;
 - b. a plurality of lipid membranes arrayed on said substrate in physically separate corrals defined by barriers on the substrate, each corral sized to contact a plurality of cells moving from corral to corral;
 - c. said lipid membranes forming, in each corral, a continuous, fluid sheet; and
 - d. dopant molecules, present within some but not all membrane sheets of the micro-array, each molecule movable within its sheet, said dopant molecules selected for cell adhesion properties that change the binding property of the lipid membrane towards the selected cell.
2. (Cancelled) The micro-array device of claim 1, wherein said dopant molecule is selected from the group consisting of:
 - a. lipids;
 - b. cell adhesion proteins of the immunoglobulin superfamily; and
 - c. selectins.

Appl. No.: 10/076,727
Amdt. Dated: 10/3/2005
Off. Act. Dated: 8/3/2005

3. (Cancelled) The micro-array according to claim 2, further comprising a layer of water separating the substrate from the membranes.
4. (Cancelled) The micro-array according to claim 3, further comprising means for immersing the micro-array within a mixture of cells and culture fluid.
5. (Cancelled) The micro-array according to claim 1, wherein the membrane lipid is phosphatidylcholine.
6. (Cancelled) The micro-array according to claim 1, wherein the membrane lipid and/or the dopant is selected from the group consisting of phosphatidylserine, dipalmitoylphosphatidic acid, distearoylphosphatidylglycerol, phosphatidylinositol, 1,2-dioleoyl-3-dimethylammonium-propane, 1,2-dioleoyl-3-trimethylammonium-propane, dimethyldioctadecylammonium bromide, 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine, N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine ammonium salt, and N-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolmine triethylammonium salt.
7. (Currently Amended) A method for screening living cell adhesion on a solid substrate comprising:
 - a. contacting a cell suspension with a micro-array comprising a substrate comprising an array of adjacent membrane corrals, wherein the corrals comprise lipid membrane lipids bilayer membranes, said lipid bilayer membranes and doped with positively or negatively one or more charged lipid lipids dopants to form a doped lipid bilayer membrane; and
 - b. observing cell adhesion to the doped lipid bilayer membranes after a time period of at least one hour.
8. (Currently Amended) A method for determining the cell adhesion properties of a living adherent cell, comprising:
 - a. providing a micro-array device having a plurality of lipid bilayer membranes disposed on a solid substrate in corrals separated by a barrier material, said lipid bilayer membranes having different compositions in different

Appl. No.: 10/076,727
Amdt. Dated: 10/3/2005
Off. Act. Dated: 8/3/2005

- corrals, wherein at least one membrane corral comprises a lipid bilayer membrane comprising one or more charged lipid dopants;
- b. culturing a population of cells in said micro-array device; and
 - c. determining the adhesion of the cells to the lipid bilayer membranes in different corrals by observing cell adhesion in response to said lipid bilayer membranes having different compositions.
9. (Currently Amended) The method according to claim 8, wherein the micro-array comprises membranes supported by a solid substrate, and wherein the one or more of said lipid bilayer membranes are doped with phosphatidylserine negatively or positively charged lipids.
10. (Currently Amended) The method according to claim 9, wherein the solid substrate is separated from the doped lipid bilayer membranes by a water layer and further comprising a material separating individual membrane corrals to permit a lateral diffusion of lipids within each corral, thereby enabling use of different membrane compositions for different corrals.
11. (Original) The method according to claim 10, wherein the substrate is a micropatterned glass wafer.
12. (Original) The method according to claim 11, wherein the membrane is an egg-phosphatidylcholine membrane.
13. (Previously Presented) The method according to claim 12, wherein the dopant lipid is selected from the group consisting of phosphatidylserine, dipalmitoylphosphatidic acid, distearoylphosphatidylglycerol, phosphatidylinositol, 1,2-dioleoyl-3-dimethylammonium-propane, 1,2-dioleoyl-3-trimethylammonium-propane, dimethyldioctadecylammonium bromide, 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine, N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine ammonium salt, and N-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolmine triethylammonium salt.
14. (Currently Amended) An assay to screen and observe differential cell adhesion of living cells to membranes comprising:

Appl. No.: 10/076,727
Amdt. Dated: 10/3/2005
Off. Act. Dated: 8/3/2005

- a. providing a micro-array of membranes in corrals displayed on a solid substrate, wherein the corrals contain lipid bilayer membranes comprised of different membrane composition elements of lipids, charged dopant lipids, proteins, and other membrane-associated molecules; then
 - b. contacting and exposing a living cell suspension with the lipid bilayer membranes disposed on the micro-array and allowing a random diffusion of the living cells on the membrane; and
 - c. observing cell adhesion to the lipid bilayer membranes over a time period.
15. (Original) The assay according to claim 14, wherein the membrane composition elements are sufficiently small to allow the cells to randomly sample many membrane elements before adhering to one.
16. (Previously Presented) The assay according to claim 15, wherein the membrane composition elements are approximately 1 micron to approximately 1 millimeter in size.
17. (Currently Amended) The assay according to claim 16, wherein the solid substrate of the micro-array is separated from the membranes by a water layer and further comprising a material separating membrane corrals, thereby permitting a lateral diffusion of membranes only within each corral.
18. (Original) The assay according to claim 17, wherein the micro-array substrate is a micropatterned glass wafer.
19. (Currently Amended) The assay according to claim 17, wherein the dopant lipid is selected from the group consisting of phosphatidylserine, dipalmitoylphosphatidic acid, distearoylphosphatidylglycerol, phosphatidylinositol, 1,2-dioleoyl-3-dimethylammonium-propane, 1,2 dioleoyl-3-trimethylammonium-propene, dimethyldioctadecylammonium bromide, 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine, N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine ammonium salt, and N-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolmine triethylammonium salt.

Appl. No.: 10/076,727
Amtd. Dated: 10/3/2005
Off. Act. Dated: 8/3/2005

20. (Currently Amended) The assay according to claim 17, wherein the lipid bilayer membrane is an egg-phosphatidylcholine membrane.
21. (Cancelled) A membrane bilayer surface comprised of:
a plurality of phosphatidylserine-free small unilamellar vesicles that have been deposited on a membrane compatible surface to form a cell adhesion-free phospholipid bilayer surface.
22. (Cancelled) The membrane bilayer surface of claim 21 wherein said cell adhesion-free phospholipid bilayer surface is an interior capillary wall of a microfluidic device to provide a cell adhesion-free microfluidic device.
23. (Cancelled) A patterned surface comprised of:
a plurality of variously doped and undoped small unilamellar vesicles bonded to a membrane compatible surface in a pattern to form a patterned cell adhesion and non-cell-adhering phospholipid bilayer surface.
24. (Cancelled) The patterned surface of claim 23 wherein said patterned cell adhesion and non-cell-adhering phospholipid bilayer surface is further measured to detect the presence, absence, or quantity of cells present on said surface.